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November 15, 1995

To: Examiner Kathleen Fonda
Group Art Unit 1803
Assistant Commissioner of Patents
Washington, D.C. 20231

From: Kevin L. Bastian
Client Number: 014137-000550US At FAX Number: **(703) 308-4227**
Number of Pages (including this page): 14

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By _____

PATENT

Attorney Docket No. 014137-000550

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
PAULSON ET AL.	Examiner: Kathleen K. Fonda
Serial No.: 08/063,181	Art Unit: 1803
Filed: May 14, 1993	COMMUNICATION
For: INHIBITORS OF INTERCELLULAR ADHESION AND THEIR USES	

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants hereby request that the suggestion under 35 USC §135(a) to copy the claim identified in the Office Action mailed October 19, 1995 be withdrawn. Applicants' representative acknowledges with appreciation the courtesies extended by the Examiner in the interview on Monday, November 13, 1995. During the interview, the suggested claim identified on page 3 of the Office Action was discussed. As pointed out at the time, the suggested claim does not correspond exactly to claim 6 of the U.S. Patent NO. 5,428,025 (the '025 patent).

Claim 6 of the '025 patent is directed to methods of treating inflammation using a tetrasaccharide consisting of the minimal SLe^x structure. Claim 6 recites that, in the structure of claim 1, n is 1, K is fucose, J is hydrogen, G is hydrogen and F is N-acetylneuraminic acid. As explained during the interview, the structure of claim 6 consists of only four monosaccharide residues.

The suggested claim, in contrast, is directed to methods using a pentasaccharide consisting of the minimal SLe^x structure plus an additional galactose residue

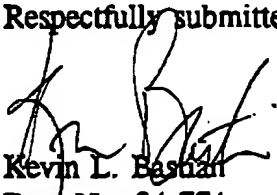
linked to the reducing end of the oligosaccharide. Moreover, as noted during the interview, the '025 patent contains no disclosure that would support a claim to a method of treating inflammation using a pentasaccharide.

During the interview the Examiner acknowledged that an inadvertent oversight may have led to the suggestion of this claim, instead of a claim directed to a method using a tetrasaccharide. It was suggested that a formal request to withdraw the part of the Office Action referring to the suggested claim be submitted. Applicants hereby submit this request. Based on the interview Applicants understand that this request will be favorably considered.

Moreover, applicants submit with this communication, a communication under 37 CFR §1.607 requesting that an interference be declared between this application and the '025 patent. As discussed during the interview, the §1.607 communication contains a proposed Count, identifies those claims in this application and the '025 patent that correspond to the proposed Count, and identifies a series of parent applications to establish applicants' senior party status.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (415) 543-9600.

Respectfully submitted,



Kevin L. Bastian
Reg. No. 34,774

TOWNSEND and TOWNSEND and CREW
One Market Plaza
Steuart Street Tower, 20th Floor
San Francisco, California 94105

(415) 543-9600
Fax (415) (543-5043)

KLB:

I hereby certify that this correspondence is being sent by facsimile transmission to: Examiner Kathleen K. Fonda
Fax No.: 1-703-308-4227
Assistant Commissioner for Patents,
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By David Kare

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PATENT

Attorney Docket No. 014137-000550

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
PAULSON ET AL.	Examiner: Kathleen K. Fonda
Serial No.: 08/063,181	Art Unit: 1803
Filed: May 14, 1993	COMMUNICATION PURSUANT TO 37 C.F.R. § 1.607
For: INHIBITORS OF INTERCELLULAR ADHESION AND THEIR USES	

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Under the provisions of 37 C.F.R. § 1.607, Applicants request that an interference be declared between the present Application Serial No. 08/063,181 and U.S. Patent No. 5,428,025, issued June 27, 1995, which is less than one year from the filing of this communication, to Brian K. Brandley et al. (the "'025" patent).

According to 37 CFR §1.601(i), an interference may be declared between a pending application and an unexpired patent when, in the opinion of the Examiner, the application and the patent contain claims for the same patentable invention. As shown in the following claim correspondence, the present application and the '025 patent contain claims to the same patentable invention.

An appropriate count for the interference is one which is as broad as the broadest claim (Claim 1) of the '025 patent as well as the broadest allowed claim (Claim 99) of this application. In view of the different approaches embodied in the actual claims presented by the parties, a phantom count is required. A suitable phantom count would be one presenting the language of the '025 patent, Claim 1, and the language of the present

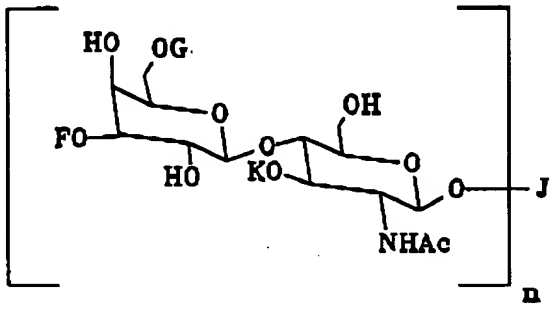
application Claim 99, with the word "or" between the two. See MPEP Section 2309.01, Example 7.

Applicants thus propose the following Count for the interference:

PROPOSED COUNT:

A method of treating inflammation, comprising:

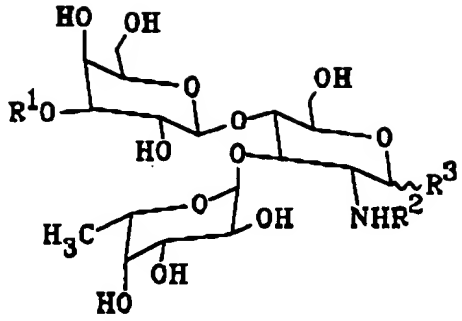
administering to a patient a therapeutically effective amount of a compound having the following general structural formula:



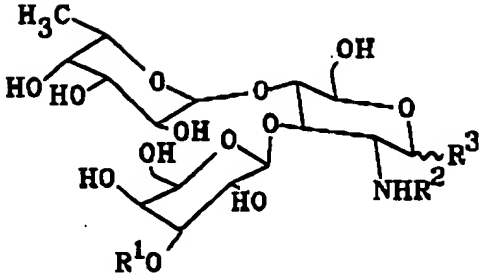
wherein one of F and G is hydrogen and one is an N-acetyl neuraminic acid residue on the terminal unit and are both hydrogen on any other unit; J is hydrogen or a linking group and K is hydrogen or a fucose residue and n is an integer of from 1 to 10 with the proviso that n and K are defined such that at least one K is a fucose residue;

or

a method for inhibiting selectin-mediated intercellular adhesion in a mammal, the method comprising administering to the mammal a therapeutically effective dose of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound which selectively binds P-selectin or E-selectin, wherein the compound is selected from the group consisting of compounds of formula I and compounds of formula II,



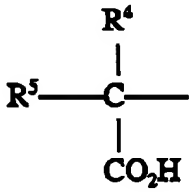
I



II

in which:

R^1 is selected from the group consisting of a sialic acid and a group having the formula III



III

in which:

R^4 and R^5 taken individually are the same or different and are selected from the group consisting of H, C_1-C_8 alkyl, hydroxy-(C_1-C_8 alkyl), aryl-(C_1-C_8 alkyl), and (C_1-C_8 alkoxy)-(C_1-C_8 alkyl), substituted or unsubstituted, or

R^4 and R^5 form a single radical which is selected from the group consisting of

---R^6--- and ---$(R^7)_q$---O---$(R^8)_r$---

in which R^6 is C_3-C_7 divalent alkyl, substituted or unsubstituted, R^7 and R^8 are the same or different and are C_1-C_6 divalent alkyl, substituted or unsubstituted, and q and r are the same or different and are zero or 1 such that the sum of q and r is at least 1;

the substitutions in the substituted groups being selected from the group consisting of hydroxy, hydroxy(C_1-C_4 alkyl), polyhydroxy(C_1-C_4, alkyl), and alkanoamido;

R^2 is selected from the group consisting of (C_1-C_8 alkyl)carbonyl, (C_1-C_8 alkoxy)carbonyl, (C_2-C_9 alkenyloxy)carbonyl;

R^3 is selected from the group consisting of an oligosaccharide, a monosaccharide, H, OH, C_1-C_{20} alkyl, C_1-C_{20} alkoxy, aryl-(C_1-C_8 alkyl), (C_1-C_8 alkyl)-aryl, and alkylthio.

Under 37 CFR §1.607(a)(3) and (4), applicants must identify at least one claim in the '025 patent and at least one claim in this application that corresponds to the proposed count. A claim corresponds to the count if it defines the "same patentable invention" as a claim that corresponds to the count. A first claim defines the same patentable invention as a second claim if the first claim is the same as (35 USC §102) or obvious (35 USC §103) in view of the second claim, assuming the second claim is prior art with respect to the first claim (37 CFR §1.601(n)).

Claim 1 of the '025 patent is identical to the first part of the proposed Count and thus corresponds exactly to the proposed Count. Claims 2-6 of the '025 patent, although not identical to the proposed Count, do not define a separate patentable invention from that defined by claim 1 and thus correspond substantially to the Count. Claim 2-6 are all dependent from claim 1 and appear to be directed to preferred embodiments of the invention defined by claim 1. Claim 2 is directed to methods using tetrasaccharides based on the

structure of claim 1, in which K is fucose. Claim 3 is directed to methods in which J is H. Claim 4 is directed to methods in which J is a linking group. Possible linking groups are disclosed in column 8, lines 26-31. Claim 5 is directed to methods in which G is H and F is N-acetylneuraminic acid; thus the claimed structures comprise an α2,3 linkage between the N-acetylneuraminic acid and the galactose residues. Claim 6 is directed to methods using the SLe^x tetrasaccharide structure. There is no evidence that the particular species or subgenera defined by these claims are surprisingly effective, or otherwise separately patentable from other members of the genus defined by claim 1 of the '025 patent. Thus, claims 2-6 correspond substantially to the proposed Count.

In the present application, claim 99 is identical to the second part of the proposed Count and thus corresponds exactly. Claims 100-108 and 120-127 correspond substantially to the Count. Claims 100-108 are directed to methods using compounds having particular structures. Claims 120-123 are directed to methods using particular pharmaceutical compositions. Claims 124-127 are directed methods of treating particular conditions using the claimed compounds.

Under 37 CFR §1.601 (j) an interference-in-fact exists when at least one claim of a party that corresponds to the count and a claim of the other party that also corresponds to the count define the same patentable invention. As noted above, claim 6 of the '025 patent is directed to an SLe^x tetrasaccharide unit. Formula I of claim 99 corresponds to the two monosaccharide residues of claim 1 of the '025 patent, with the addition of a fucose residue linked to the glucosamine residue. If in claim 99, R^1 is sialic acid (NeuAc), R^2 is C_1-C_8 alkyl carbonyl (which includes acetyl), and R^3 is OH, an SLe^x tetrasaccharide structure is obtained. Thus, claim 99 of the present application is directed to a genus which includes the species defined by claim 6 of the '025 patent.

It is well settled that a claim to a genus is always anticipated by a prior disclosure of a species or subgenus within the genus. Claim 6 of the '025 patent anticipates claim 99 of the present application, assuming claim 6 is prior art to it. In addition, in the absence of surprising results, claim 6 of the '025 patent is obvious over claim 99 of the

present application, assuming claim 99 is prior art. These claims therefore define the same patentable invention. An interference between the present application and the '025 patent should therefore be declared.

Claims 109-119 of the present application are directed to inhibition of intercellular adhesion using oligosaccharide compounds consisting of 5 or 6 monosaccharide units. These claims are directed to a separately patentable invention from the other claims that correspond to the Count and thus do not correspond to the Count. As explained below, claims 109-119 are not obvious in view of the other claims corrseponding to the proposed Count because they are directed to methods which are surprisingly effective in inhibiting selectin-mediated intercellular adhesion and that are not disclosed nor suggested by the other claims.

It is well established that evidence of surprising or unexpected results can be used to establish that a claimed invention is not obvious over the prior art[1]. *In re Soni* 34 USPQ2d 1685 (1995). The specification contains strong evidence of the unexpected properties of hexasaccharides and pentasaccharides in claims 109-119. In particular, in the experiments described in Example 7 (pages 71-73) oligosaccharides comprising the minimal SLe^x tetrasaccharide structure as well as oligosaccharides comprising one (pentasaccharides) or two (hexasaccharides) additional monosaccharide units were prepared. The ability of each of these compounds to inhibit P-selectin mediated intercellular adhesion was then measured in the adhesion assay described in Example 5 (page 67-69).

The results of these experiments are shown in Table 2 on page 73. As shown there and explained on page 73, approximately 20 times more tetrasaccharide was required for 50% inhibition than either the hexasaccharide or the pentasaccharide. Thus, these experiments indicate that the addition of one or two additional monosaccharides to the tetrasaccharide provide dramatically increased affinity for the target receptor. As a result, less of these compounds is required to inhibit intercellular adhesion.

Further evidence that claims 109-119 are separately patentable is the absence of any disclosure of such structures in the '025 patent. Thus, the '025 patent neither

[1] In this case, the claims corresponding to the proposed Count are the prior art.

discloses nor suggests that such structures are particularly preferred or are surprisingly effective.

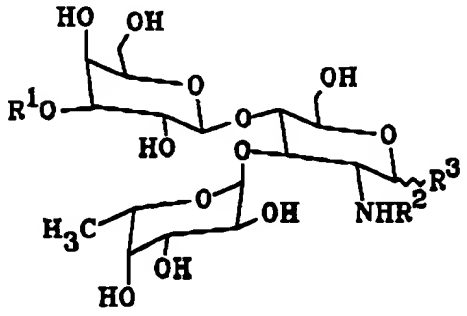
Pursuant to 35 U.S.C. §120 and 37 C.F.R. §1.78, application claims 99-127 should be given the benefit of the filing date of application 07/538,853, filed June 15, 1990 through a chain of applications as set out below. These applications are each a constructive reduction to practice of the proposed Count.

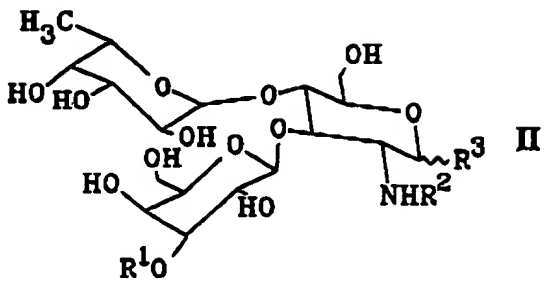
08/063,181, filed 5/14/93
is a CIP of
07/810,789, filed 12/17/91, abandoned 10/16/93,
which is a CIP of
07/716,735, filed 6/17/91, abandoned 2/3/93,
which is a CIP of
07/632,390, filed 12/20/90, abandoned 6/10/92,
which is a CIP of
07/619,319, filed 11/28/90, abandoned 8/29/91,
which is a CIP of
07/538,853, filed 6/15/90, abandoned 1/3/91.

All of these applications name common inventors. Each application was filed during the pendency of its immediate parent application. Thus, the requirements of 35 USC §120 have been met for each CIP application.

The language of the proposed Count, which corresponds exactly to claim 99 of the above-captioned application, as applied to priority application 07/538,853, as set forth below, shows that the priority application, as well as each of the applications in the above-recited chain of applications, is a constructive reduction to practice of the proposed Count.

Count (Claim 99)	the '853 application
A method for inhibiting selectin-mediated intercellular adhesion in a mammal	"[T]he compositions act to inhibit intercellular adhesion mediated by the selectin cell surface receptor . . . the invention methods of inhibiting intercellular adhesion in a patient . . ." (See page 3, lines 10-11 and lines 18-19.)

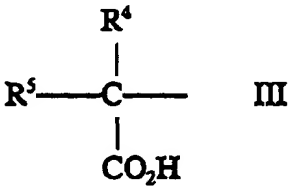
the method comprising administering to the mammal a therapeutically effective dose of	". . . by administering to the patient a therapeutically effective dose of . . ." (See page 3, lines 21-22.)
a pharmaceutical composition comprising a pharmaceutically acceptable carrier and	"Preferably, the pharmaceutical compositions are administered intravenously. Thus, this invention provides compositions for intravenous administration which comprise a solution of the compound dissolved or suspended in an acceptable carrier." (See page 19, lines 33-37.)
a compound which selectively binds E-selectin	". . . a moiety capable of binding a selectin cell surface receptor. The cell surface receptor, such as ELAM-1, may be expressed on vascular endothelial cells." (See page 3, lines 22-25.)
wherein the compound is selected from the group consisting of compounds of formula I and formula II:  I	"NeuAcα2,3Galβ1,4(Fucα1,3) GlcNacβ1-R_1; wherein R_1 is an . . . oligosaccharide." (See page 3, lines 28-29.) Formula I of the Count corresponds to the three monosaccharide residues Galβ1,4(Fucα1,3) GlcNac disclosed in the structure of the text quoted above. The disclosure of this structure is a constructive reduction to practice of the count when, in Formula I of the count, R^1 is sialic acid (NeuAc), R^2 is C_1-C_8 alkyl



II

in which:

R^1 is selected from the group consisting of a sialic acid and a group having the formula III



III

in which:

R^4 and R^5 taken individually are the same or different and are selected from the group consisting of H, C_1-C_8 alkyl, hydroxy-(C_1-C_8 alkyl), aryl-(C_1-C_8 alkyl), and (C_1-C_8 alkoxy)-(C_1-C_8 alkyl), substituted or unsubstituted, or

R^4 and R^5 form a single radical which is selected from the group consisting of

—R^6— and —(R^7)$_q$—O—(R^8)$_r$—

in which R^6 is C_3-C_7 divalent alkyl, substituted or unsubstituted, R^7 and R^8 are the same or different and are C_1-C_6 divalent alkyl, substituted or unsubstituted, and q and r are the same or different and are zero or 1 such that the sum of q and r is at least 1;

the substitutions in the substituted groups being selected from the group consisting of hydroxy, hydroxy(C_1-C_4 alkyl), polyhydroxy(C_1-C_4, alkyl), and alkanoamido;

R^2 is selected from the group consisting of (C_1-C_8 alkyl)carbonyl, (C_1-C_8 carbonyl (which includes acetyl), and R^3 is an oligosaccharide.

alkoxy)carbonyl, (C_2-C_9 alkenyloxy)carbonyl;

R^3 is selected from the group consisting of an oligosaccharide, a monosaccharide, H, OH, C_1-C_{20} alkyl, C_1-C_{20} alkoxy, aryl-(C_1-C_8 alkyl), (C_1-C_8 alkyl)-aryl, and alkylthio.

This language is found in each of the subsequent applications. The present application incorporates the disclosure of each of the previous applications by reference, including the immediate parent application, the '789 application. The '789 application incorporates the '390 application by reference and was filed while the '390 application was pending. The '390 application incorporates the '853 application by reference and was filed while the '853 application was pending. Thus, the language found in the '853 application noted above has been incorporated by reference into the present application.

The '853 application, which is applicants' priority application, is a constructive reduction to practice of the proposed Count. Therefore, Applicants are entitled to an effective filing date of June 15, 1990. This date is earlier than the claimed priority date of the '025 patent, July 30, 1990. Because Applicants have the earliest effective filing date as to the proposed Count, Applicants should be named senior party. 37 C.F.R. § 1.601(m) and § 1.611(c).

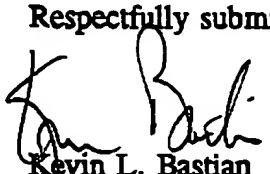
The claims in this application were added by preliminary amendment filed April 19, 1994. As explained in the amendment, support for claims 99-127 is found primarily in the claims as originally filed. Specific support for formula II of claim 99 is found on page 13, lines 3 to 10. Specific support for claim 114, and the claims which depend from it, is found in the structures presented in Figure 12B. Specific support for claim 121 at page 47, lines 36-37. Specific support for claim 123 is found at page 49, lines 35-39. It is further noted that the preliminary amendment has been entered and these claims have been indicated as being allowable. Thus, the requiremnts of 37 CFR §1.607(a)(5) and (6) have also been met.

PATENT

Applicants respectfully submit that all of the requirements of 37 CFR §1.607(a)(1)-(6) have been met and that an interference should be declared betwen the present application and the '025 patent with applicants named as senior party.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (415) 543-9600.

Respectfully submitted,



Kevin L. Bastian
Reg. No. 34,774

TOWNSEND and TOWNSEND and CREW
One Market Plaza
Steuart Street Tower, 20th Floor
San Francisco, California 94105

(415) 543-9600
Fax (415) (543-5043)

KLB:

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